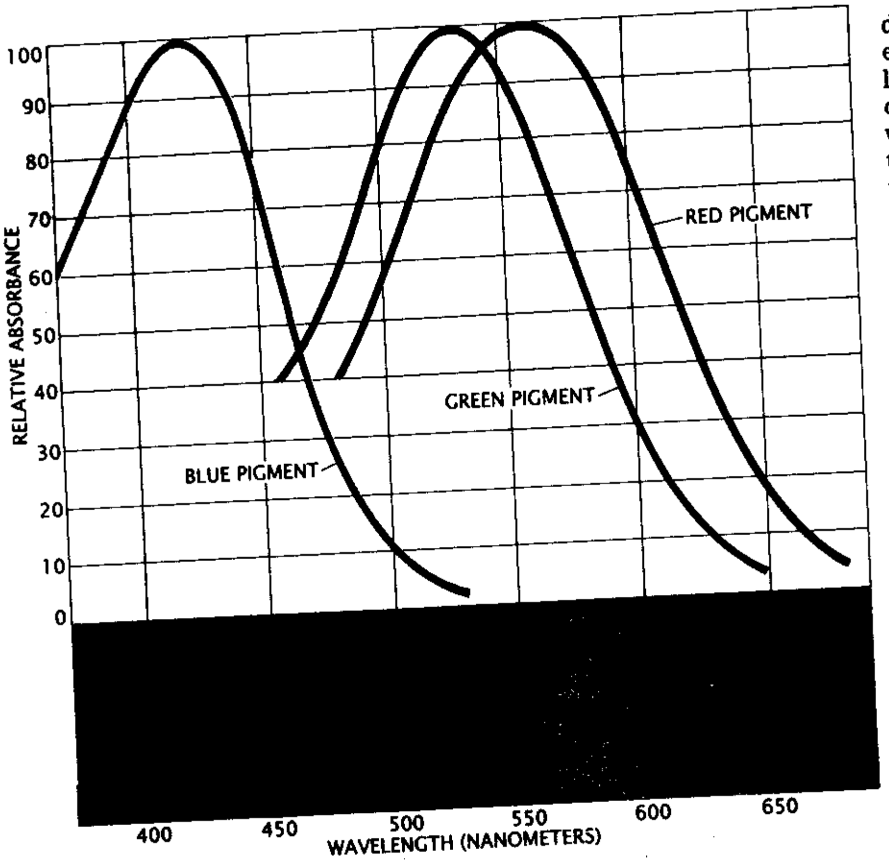


SPECTRAL-SENSITIVITY CURVES show the sensitivity of the three color pigments to the visible spectrum of light. The curves were plotted on the basis of data obtained by James K. Bowmaker of the University of London and H. J. A. Dartnall of the University of Sussex. What is called the blue pigment is particularly responsive to the short-wavelength region of the spectrum; the green and red pigments are more sensitive to intermediate and long wavelengths. The pigments themselves have still not been isolated; hence Bowmaker and Dartnall determined their sensitivities by measuring the light absorbed by individual cones that were obtained from cadavers.

lights are detected by a single class of receptors; by adjusting the intensity of a single light, a dichromat can always equalize the number of photons captured from the two sides of the screen.

Such differences between normal subjects and red$^-$ and green$^-$ dichromats enabled Rayleigh to readily pick out the dichromats with his new device. He also identified two additional groups of color-variant subjects by testing his friends and relatives. Like normal subjects (and unlike the dichromats), these variant individuals required some mixture of red and green lights to match the yellow, but they chose unusual ratios. One group required more green and less red; the other group required the reverse. Rayleigh concluded that these subjects, now known as green-anomalous and red-anomalous trichromats, had green or red receptors with atypical spectral sensitivities.

By the mid-20th century such psychophysical studies, which depended on the judgment of subjects, strongly supported Young's three-receptor theory, and other studies had suggested that the cone cells of the retina served as those receptors. Finding direct proof for these ideas remained technically challenging, however. One major obstacle was that the cones were difficult to isolate. They are intermingled throughout the retina with the much more numerous rod cells, photoreceptors responsible for black-and-white vision in dim light.

Nevertheless, ingenuity won out. In the 1960's Paul K. Brown and George Wald of Harvard University and Edward F. MacNichol, Jr., William H. Dobelle and William B. Marks of Johns Hopkins University built microspectrophotometers capable of determining the absorbance of a single photoreceptor cell. The device passes a variable-wavelength light (one whose wavelength is changeable) through the color-detecting region of a cone and passes an identical beam through a different region, testing wavelengths across the spectrum; the difference in the intensity of the emerging beams at a specific wavelength is a measure of the absorbance of the color-detecting region at that wavelength. The studies employing the device demonstrated that cones taken at autopsy from human retinas did indeed exhibit three distinct absorbance spectra. The observed spectra agreed well with the sensitivities predicted by psychophysical studies.

A plot of the relative fraction of photons absorbed per second by each class of cones against the wavelengths of the visible spectrum yields three bell-shaped curves. The blue cones absorb wavelengths ranging from 370 nanometers (billionths of a meter) to 530 nanometers and are most sensitive to wavelengths of 420 nanometers. Both the green and the red cones are active across most of the spectrum but are particularly sensitive to wavelengths between about 450 and 620 nanometers. The green cones are most efficient at 535 nanometers, the red cones at 565 nanometers.

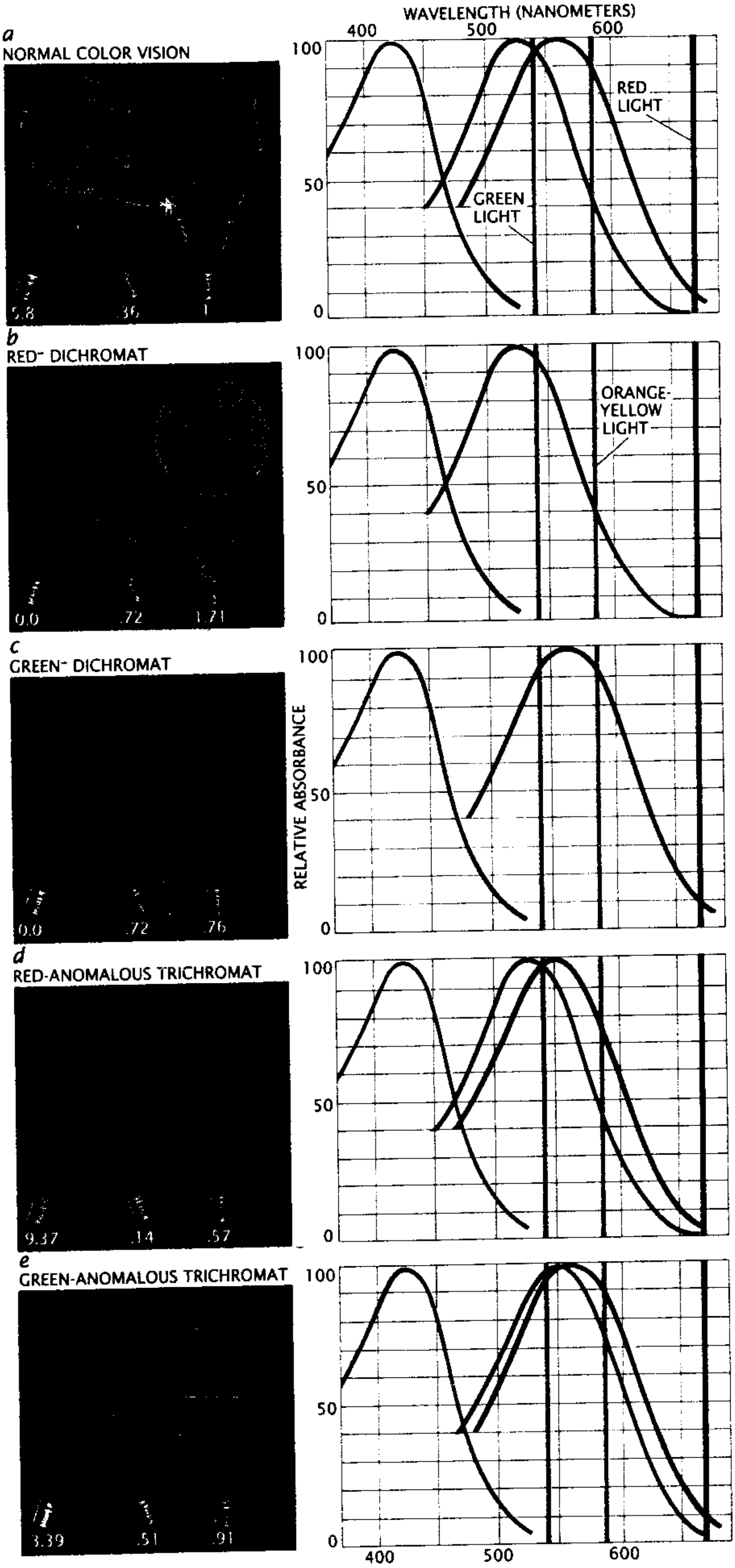
Beginning in the 1970's new evidence that dichromats lack one or another class of receptors emerged. William A. H. Rushton of the University of Cambridge directed a variable-wavelength light into the eyes of dichromats and measured the light reflected from—and hence not absorbed by—the retina; he thereby demonstrated that specific wavelengths are not absorbed normally by dichromats. More recently, James K. Bowmaker of the University of London, John D. Mollon of Cambridge and H. J. A. Dartnall of the University of Sussex showed with a microspectrophotometer that a retina obtained from a green$^-$ dichromat did not have the green class of cones.

New evidence also yielded clues to the basis of anomalous trichromacy. By means of psychophysical techniques Rushton and, separately, Thomas P. Piantanida and Harry G. Sperling, who were then at the University of Texas, demonstrated that the spectral-sensitivity curves of anomalous red and green receptors lie in the interval between the normal red and green absorbance curves.

With the existence of three distinct classes of cones firmly established, in the early 1980's my colleague David S. Hogness and I turned our attention to the genetic bases of normal and abnormal color vision. In addition to aiding in the effort to isolate the pigment proteins, we hoped to supplement the findings of classical genetic studies that traced the inheritance of aberrant color vision within families.

Such studies built on the old observation that deficiencies in red-green discrimination are commoner in males than in females. Analysis of this pattern indicated that genes on the X (sex) chromosome are responsible for the variation. Males will have variant red-green discrimination if their single X chromosome (inherited from the mother) carries the trait; females will be affected only if they receive a variant X chromosome from both parents. The studies also indicated that variations in blue sensitivity are rooted in a gene on some nonsex chromosome. We planned to test the most straightforward explanation for these inheritance patterns, namely that color-vision variations result from inherited alterations in the genes encoding the cone pigments. Presumably mutations in such genes could result in the loss of a functional pigment or in the production of a pigment with an abnormal absorbance spectrum.

Our approach involved isolating the genes that code for the color pigments and comparing their structures in people with normal and variant color vision. Frequently one isolates genes by determining the amino acid sequences of the proteins they encode and parlaying that information into clues about the structure


a NORMAL COLOR VISION

b RED⁻ DICHROMAT

c GREEN⁻ DICHROMAT

d RED-ANOMALOUS TRICHROMAT

e GREEN-ANOMALOUS TRICHROMAT

COLOR MATCHES (*left*) made in a test of red-green color discrimination are depicted next to the subjects' spectral-sensitivity curves (*right*). The testing device, a Rayleigh anomaloscope, superposes a red and a green light on one half of a white screen and projects an orange-yellow light onto the other half. Subjects adjust the ratio of red light to green and the intensity of the yellow light until the two sides of the screen appear to match—that is, until the light absorbed by each type of pigment from one side of the screen is equal to the amount absorbed from the other side. The numbers below the lights show the relative intensities. Normal subjects (*a*) require both the red and the green light to match the yellow, choosing a high intensity of red and a low intensity of green. (The red and green pigments both absorb the red light less efficiently and the green light more efficiently than they do the yellow.) People who lack the red (*b*) or the green (*c*) pigment are identified by their ability to match the yellow light with the red or the green alone. (Only the green matches are shown.) Subjects whose red (*d*) or green (*e*) pigments have abnormal spectral sensitivities require both red light and green light to match the yellow but, compared with normal subjects, choose an excess of red or green respectively.